Answer 1:

Bibliographic Information

Fundamental study of combination chemotherapy with THP, 5-FU and CDDP for human KB carcinoma cell line and its multidrug resistant cell line KB-C1-usefulness of treatment with 5-FU preceding CDDP. Kishimoto, Hiromitsu; Manno, Yukiyo; Tanaka, Hitoshi; Moridera, Kuniyasu; Urade, Masahiro. Department of Density and Oral Surgery, Hyogo College of Medicine, Japan. Gan to Kagaku Ryoho (2001), 28(4), 505-509. Publisher: Gan to Kagaku Ryohosha, CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 135:338793 AN 2001:332577 CAPLUS

Abstract

This study was designed to investigate the usefulness of treatment with 5-FU preceding CDDP in combination chemotherapy with THP, 5-FU and CDDP. Using the human KB carcinoma cell line and its multidrug resistant cell line KB-C1, the difference in the antitumor effect due to the sequence of administration of CDDP and 5-FU (TCF or TFC) was examd. on culture cells and nude mouse tumor xenografts. When KB and KB-C1 were treated with THP (0.01μg/mL) on day 1, CDDP (0.05μg/mL) on day 2 or day 4 and 5-FU (0.25μg/mL) on day 3 and 4 or day 2 and 3. TFC suppressed the cell proliferation more strongly than TCF ($p<0.05$), though there was no difference between KB and KB-C1. In nude mouse xenografts, i.p. administration of THP (0.5 mg/kg) on day 1, CDDP (2 mg/kg) on day 2 or 5, and 5-FU (10 mg/kg) on day 3-5 or day 2-4 inhibited tumor growth more effectively in KB than in KB-C1. At three weeks postadministration, growth inhibition by TCF and TFC was 29.9% and 57.4% in KB and 25.5% and 49,8% in KB-C1, resp. Theses results indicate that TFC was superior to TCF in cytocidal and antitumor effects for KB and KB-C1.

Answer 2:

Bibliographic Information

Activity of menogaril against various malignant lymphoma cell lines and a human lymphoma xenograft in mice. Yoshida, Masahiko; Fujioka, Akio; Nakano, Koushi; Yuasa, Chie; Toko, Toshiyuki; Takeda, Setsuo; Unemi, Norio. Anticancer and Antimicrobials Research Laboratory, Taiho Pharmaceutical Co., Ltd., Tokushima, Japan. Anticancer Research (1996), 16(5A), 2875-2880. Publisher: Anticancer Research, CODEN: ANTRD4 ISSN: 0250-7005. Journal written in English. CAN 126:591 AN 1996:703966 CAPLUS

Abstract

Menogaril is an antitumor agent different from other anthracyclines in that it is active after oral administration; therefore, extravasation is not a side effect. In this basic study, we examd. the antitumor activity of menogaril against malignant lymphoma. We compared its activity towards exptl. malignant lymphoma with that of Adriamycin, epirubicin, pirarubicin vincristine, and etoposide, treating mice with each drug at the dose schedule usually used for patients. Menogaril rapidly penetrated lymphoma cells and remained there at least 3 h after the drug was washed out. Menogaril cleaved more double-stranded DNA in lymphoma cells than Adriamycin, epirubicin, pirarubicin, or etoposide. Menogaril had stronger antitumor activity against exptl. malignant lymphoma in mice than Adriamycin, epirubicin, vincristine, and etoposide. Menogaril significantly lengthened the life span of mice bearing one of three lymphoma cell lines resistant to cisplatin, vincristine, or cyclophosphamide. Menogaril had stronger antitumor activity against the human malignant lymphoma xenograft LM-3 than adriamycin. The strength of the cytotoxic activity of Menogaril might arise from its ready penetration into cells and its cleavage of double-stranded DNA. Therefore, Menogaril might become a drug for the treatment of patients with malignant lymphoma by oral administration; 7 days of administration was active in the in vivo expts.

Answer 3:

Bibliographic Information

In vivo/in vitro correlation of xenografts in nude mice and the ATP-cell viability assay. Perras, James P.; Hurst, Josephine.

School Medicine, University Miami, Miami, FL, USA. Contributions to Gynecology and Obstetrics (1994), 19(Chemosensitivity Testing in Gynecologic Malignancies and Breast Cancer), 122-131. Publisher: Karger, CODEN: CGOBD6 ISSN: 0304-4246. Journal written in English. CAN 125:131526 AN 1996:450444 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The authors compare in vitro results of an ATP cell viability assay (ATP-CVA) to the in vivo chemosensitivity of transplanted ovary and breast xenografts in nude mice. This approach not only allows a comparison between the in vitro and in vivo systems, but it also provides a means to compare responses using multiple tumor specimens to evaluate the reproducibility of the ATP- CVA. The results strongly indicate that the ATP-CVA in vitro chemosensitivity assay provides an approach that, to a degree, approximates a clin. situation. With this method, the initial evaluations of in vitro chemosensitivity assays can be done more quickly and easily to compare with in vivo response. It has been shown for 2 xenograft tumors (ovarian and breast) that for those drugs tested, the ATP-CVA can predict the drug sensitivity of these tumors in nude mice. The reproducibility of the ATP-CVA assay is also demonstrated.

Answer 4:

Bibliographic Information

Characteristic antitumor activity of cytarabine ocfosfate against human colorectal adenocarcinoma xenografts in nude mice. Koga, Kunihiko; Iizuka, Eri; Sato, Akira; Ekimoto, Hisao; Okada, Mineaki. Anticancer Drugs Department, Nippon Kayaku Co. Ltd., Tokyo, Japan. Cancer Chemotherapy and Pharmacology (1995), 36(6), 459-62. Publisher: Springer, CODEN: CCPHDZ ISSN: 0344-5704. Journal written in English. CAN 124:21260 AN 1995:935559 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The antitumor activity of cytarabine ocfosfate (SPAC) was tested against human colorectal, gastric, and lung adenocarcinoma xenografts in nude mice in comparison with the activities of various antitumor drugs used clin. SPAC showed higher therapeutic efficacy against human colorectal adenocarcinoma xenografts than against human gastric and lung adenocarcinoma xenografts. SPAC was effective against three of 4 human colorectal adenocarcinoma xenografts, with efficacy higher than that of 1-β-D-arabinofuranosylcytosine, fluorouracil, cisplatin, doxorubicin, pirarubicin and vindesine sulfate, but lower than that of mitomycin C and cyclophosphamide. SPAC may be useful for inductive and/or postoperative chemotherapy against colorectal adenocarcinomas.

Answer 5:

Bibliographic Information

Evaluation of antitumor activities of topoisomerase inhibitors against neuroblastoma. In vivo study. Kaneko, Michio; Kaneko, Setsuko; Ohkawa, Haruo. Inst. Clin. Med., Univ. Tsukuba, Tsukuba, Japan. Igaku no Ayumi (1993), 165(12), 875-6. CODEN: IGAYAY ISSN: 0039-2359. Journal written in Japanese. CAN 119:85577 AN 1993:485577 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The human neuroblastoma TNB-9 and TS-N-2 and the primitive neuroectodermal tumor SK-N-AS were xenografted to Balb/c nu/nu mice. At the time when xenografts developed to 150-250 mg, the topoisomerase (TIM)-I inhibitor camptothecin-11 (CPT-11), the TIM-II inhibitor etoposide (EPS0 and its new deriv. NK-611, pirarubicin (PR), and ME-2303, a new adriamycin deriv., were administered i.p. or i.v. 3 times per 4 days at 13 LD50. Max. inhibition rates (MIR) of CPT-11 against TNB-9, TS-N-2, and SK-N-AS were 98%, 84%, and 89%, resp. As to TIM-II inhibitors, on the other hand, only ME-2303 showed an antitumor activity against TNB-9 and SK-N-AS with MIR of 59% and 64%, resp. EPS, NK-611, and PR had no antitumor activity against any tumors tested.

Answer 6:

Bibliographic Information

Experimental study on potentiation of doxorubicin (DOX) efficacy by modification of plasma transmembrane potential. Aogi, Kenjiro. Res. Inst. Nucl. Med. Biol., Hiroshima Univ., Hiroshima, Japan. Hiroshima Daigaku Igaku Zasshi (1992), 40(4), 337-52. CODEN: HDIZAB ISSN: 0018-2087. Journal written in Japanese. CAN 118:247076 AN 1993:247076 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Cell growth inhibition induced by a 30 min treatment with doxorubicin (DOX) was the greatest in K562 cells (human myelogenous leukemia cells, IC50:0.56 μM), lower in PH101 cells (human pancreatic cancer cells, 3.20 μM), and lowest in SH101 cells (human gastric cancer cells, 4.50 μm). The similar relationship was obsd. in the expts. using human tumor xenografts implanted in nude mice. Membrane potential was increased by non-toxic dose of cepharanthin (CE), a biococlaurine alkaloid, or N-1379, a isoprenoid deriv. The DOX-induced cytotoxicity was augmented by CE (K562; 1.6-fold, PH101; 10.0-fold, SH101; 6.9-fold) or N-1379 (K562; 1,2-fold, PH101; 7.8-fold, SH101; 3.5-fold), assocg. with the increases of potential, DOX accumulation, and the percentage of cells in S and G2M phases. These results suggest that plasma transmembrane potential plays an important role in DOX-induced cytotoxicity, and DOX efficacy can be potentiated by CE or N-1379 which increases transmembrane potential.

Answer 7:

Bibliographic Information

Antitumor effect of pirarubicin (THP) against human colon cancer transplanted into nude mice and the mechanism for cell cycle progression. Kataoka, Kazuhiko; Naomoto, Yoshio; Muro, Masahiko; Kojima, Kazushi; Horiki, Sadayuki; Hizuta, Akio; Tanaka, Noriaki; Orita, Kunzo. Med. Sch., Okayama Univ., Okayama, Japan. Gan to Kagaku Ryoho (1992), 19(3), 367-71. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 116:227839 AN 1992:227839 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Pirarubicin (THP) is a deriv. of adriamycin (ADM) which has been reported to have a lower cardiotoxicity than ADM. The authors investigated the in vivo antitumor effect of THP against human colon cancer cells (RPMI 4788) xenografted into nude mice. In the model of intra-abdominal carcinomatosis, i.p. administration of THP (6 mg/kg) resulted in a significant prolongation of the survival compared with the saline control group. I.v. administration of THP (8 mg/kg) significantly inhibited tumor growth compared with the saline control group. Labeling index with bromodeoxyuridine (BrdU) of RPMI 4788 tumors treated with THP was smaller than that in the control group. Mitotic index was also smaller in the group treated with THP. Labeling index with BrdU indicates the proportion of cells in the S phase. Thus, the tumor cells in both S and M phases have decreased after treatment with THP. This change in the cell cycle progression may be due to the accumulation of G2 phase similar to in vitro study. From these results, it was suggested that the change in cell cycle progression revealed in vitro might be caused by THP in vivo.

Answer 8:

Bibliographic Information

An experimental study on optimal administration of cisplatin for ovarian cancer. Akizuki, Hideaki. Sch. Med., Kurume Univ., Kurume, Japan. Kurume Igakkai Zasshi (1991), 54(5), 359-66. CODEN: KIZAAL ISSN: 0368-5810. Journal written in Japanese. CAN 115:270110 AN 1991:670110 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Antitumor effects of cisplatin (CDDP) alone and a combination of CDDP and adriamycin (ADM as pirarubicin) against ovarian cancer xenografts from a human ovarian serous cystadenocarcinoma cell line KOC-3S were evaluated in athymic mice to det. the optimal drug regimen. Adverse effects were also evaluated. The dose of ADM with antitumor effects identical to those of 8 mg/kg of CDDP and the optimal doses of ADM combined with CDDP were decided by isograph. Antitumor effects were evaluated from the tumor inhibition rate shown in the Battelle Columbus Lab. Protocol. A dose of 12 mg ADM/kg showed the same antitumor effect as 8 mg CDDP/kg. The combination of 4 mg/kg of CDDP and 6 mg/kg of ADM (CDDP/ADM ratio =2:3) yielded max. tumor inhibition rate of 68% with tolerable adverse effects. The combination of CDDP and ADM is superior to CDDP alone for optimal antitumor effects.

Answer 9:

Bibliographic Information

Predictability of preclinical evaluation of anticancer drugs by human gastrointestinal cancer-nude mouse panel. Fujita, Masahide; Fujita, Fumiko; Sakamoto, Yasuo; Sugimoto, Takuji; Shimozuma, Kojiro; Taguchi, Tetsuo. Res. Inst. Microb. Dis., Osaka Univ., Suita, Japan. Gan to Kagaku Ryoho (1991), 18(9), 1429-37. CODEN: GTKRDX ISSN: 0385-0684. Journal written in Japanese. CAN 115:269825 AN 1991:669825 CAPLUS

Abstract

The predictability of clin. responses to anticancer agents was studied using a human cancer-nude mouse panel. The human cancer lines used were 12 gastric, 4 colorectal, 3 breast, 2 pancreatic cancers and 1 melanoma xenografted into BALB/c athymic nude mice. Treatment was conducted daily 25 times for antimetabolites, and intermittently 5 times once or twice a week for other drugs. The dosage of each drug was the maximal tolerated dose predetd. for the treatment and schedule. Four weeks after the initiation of treatment, the therapeutic effect was evaluated by the tumor growth inhibition rate (IR) based on the mean tumor wt. When the IR was >58%, the drug was evaluated as effective. The clin. response rate of each drug was referred from the result of a phase II study. Direct comparison of antitumor effects on 16 tumor xenografts with responses to the corresponding clin. therapy of each donor patient revealed a fairly high accordance rate (94%). To elucidate the value of human cancer-nude mouse panel as a preclin. secondary screening, the response rates to 8 anticancer drugs used in 15 cancer xenografts were compared with the cumulative clin. data available for each drug. Generally, the response rates of the human cancer xenografts to the drugs showed fairly good correlations with the cumulative clin. response rates to the corresponding drugs in the same organs. Using this panel, preclin. examns. of 6 new agents under development, including 254-S and 2 cisplatin derivs., were performed in order to collect clin. data.

Answer 10:

Bibliographic Information

Activity of cytostatic drugs in two heterotransplanted human testicular cancer cell lines with different sensitivity to standard agents. Harstrick, Andreas; Schmoll, Hans Joachim; Casper, Jochen; Wilke, Hansjochen; Poliwoda, Hubert. Med. Sch., Univ. Hannover, Hannover, Germany. European Journal of Cancer (1990), 26(8), 898-901. CODEN: EJCAEL ISSN: 0959-8049. Journal written in English. CAN 114:220860 AN 1991:220860 CAPLUS

Abstract

Two human testicular cancer cell lines were used in a mouse xenograft model to assess the antitumor activity of 15 anticancer agents. Line H 12.1 was highly sensitive to cisplatin, bleomycin, and vinblastine, resembling non-pretreated testicular tumors, whereas line H 23.1 showed resistance to cisplatin and vinblastine, comparable to tumors with acquired or intrinsic drug resistance. In line H 12.1, several drugs were highly active, including cyclophosphamide, ifosfamide, nimustine, and vincristine. Carmustine, vindesine, doxorubicin, epidoxorubicin, pirarubicin, mitoxantrone, carboplatin, and iproplatin had only moderate activity. In line H 23.1, only cyclophosphamide, ifosfamide, animustine, vincristine, and bleomycin had an antitumor activity. The 2 cells lines represent a useful model for preclin. evaluation of new agents with presumed activity in testis cancer.

Answer 11:

Bibliographic Information

Chemosensitivity test in vivo and in vitro and cell kinetic characteristics of human lung small cell carcinoma. Inada, T.; Kubota, T.; Isobe, Y.; Fukutomi, T.; Ishibiki, K.; Abe, O. Sch. Med., Keio Univ., Tokyo, Japan. Editor(s): Ishigami, Joji. Recent Adv. Chemother., Proc. Int. Congr. Chemother., 14th (1985), Anticancer Sect. 1 373-4. Publisher: Univ. Tokyo Press, Tokyo, Japan CODEN: 55GNAX Conference written in English. CAN 105:218195 AN 1986:618195 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

The chemosensitivity of human lung small cell carcinoma (SCC) was assessed in vitro (H-69, H-128, Lu-24, and Lu-130 stains) and in vivo (Lu-24, lu-130, and lu-134 strains serially transplanted into nude mice), and the cell kinetics of SCC was analyzed in vivo. 4-Hydroxyperoxycyclophosphamide [39800-16-3] was most effective on the 4 cell lines in vitro followed by 4-O-tetrahydropyranyladriamycin [72496-41-4], adriamycin [23214-92-8], and mitomycin C (MMC) [50-07-7]. MMC was the most effective on the 3 SCC xenografts. Although the chemosensitivity pattern of SCC cell lines in vitro were similar to those of clin. reports, some discrepancy was present in the model of SCC xenografts in nude mice. This discrepancy might be partly explained by the small growth fraction of SCC in vivo. However, as the cell kinetics of SCC cells represented by short cell cycletime is well preserved in vivo. These exptl. models of SCC in vitro and in vivo appear to be suitable as a therapeutic model of SCC.

Answer 12:

Bibliographic Information

Screening test of antitumor agents by human tumor cell lines in nude mice in ascitic form. Kitahara, Takeshi; Minato, Keisuke; Shimoyama, Masanori. Natl. Cancer Cent. Hosp., Japan. Gan no Rinsho (1984), 30(9), 1158-67. CODEN: GANRAE ISSN: 0021-4949. Journal written in Japanese. CAN 102:17008 AN 1985:17008 CAPLUS (Copyright (C) 2008 ACS on SciFinder (R))

Abstract

Human breast cancer and leukemic cells implanted in nude mice appeared to be useful models for the screening of neoplasm inhibitors. The sensitivities of implanted tissues to drugs were similar to those found in patients. Studies on the suitable route of administration in these mice provide the best administration routes for humans.

Answer 13:

Bibliographic Information

Preparation and pharmacokinetics of pirarubicin loaded dehydration-rehydration vesicles. Kawano Kumi; Takayama Kozo; Nagai Tsuneji; Maitani Yoshie Institute of Medicinal Chemistry, Hoshi University, Ebara 2-4-41, Shinagawa, 142-8501, Tokyo, Japan International journal of pharmaceutics (2003), 252(1-2), 73-9. Journal code: 7804127. ISSN:0378-5173. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 12550782 AN 2003042728 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Liposomes entrapped pirarubicin (THP, L-THP) were prepared by the modified dehydration-rehydration vesicle (DRV) method, and their pharmacokinetics and antitumor effects were evaluated in mice bearing M5076 liver metastasis tumor. After small unilamellar vesicles (SUVs) composed of egg lecithin, cholesterol (Ch), beta-sitosterol beta-D-glucoside (Sit-G)

and oleic acid (OA) were freeze-dried with THP and sugars, rehydration of the lyophilized powders led to form the larger vesicles entrapping drugs, but the proper amounts of sugars and OA to lipids (sucrose/lipid=8 (w/w)) maintained the small particle size (about 340nm) with high entrapment (80.7%) of THP. After intravenous injection of L-THP, the accumulations of THP in the liver and heart were approximately 4-fold higher and half lower, respectively, than those of free THP (F-THP). L-THP had superior antitumor effect in 10mg/kg intravenous administration without significant body weight loss. L-THP is a potential drug dosage form of liver cancer treatment since the liposomes carry THP to the liver.

Answer 14:

Bibliographic Information

Docetaxel enhances the cytotoxicity of tetrahydropyranyladriamycin in a sequence-dependent manner. Egawa T; Kubota T; Furukawa T; Otani Y; Watanabe M; Furukawa T; Kumai K; Kitajima M Department of Surgery, School of Medicine, Keio University, Tokyo, Japan Anticancer research (2001), 21(4A), 2597-600. Journal code: 8102988. ISSN:0250-7005. Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 11724327 AN 2001678060 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND: Taxanes and anthracyclines are active against breast cancer. In this study we investigated the combined antitumor activity of these drugs, with particular regard to sequence-dependency. MATERIALS AND METHODS: The combined antitumor activity of docetaxel and tetrahydropyranyladriamycin (THP) against two human breast cancer xenografts was assessed using an in vitro histoculture drug-response assay. The sequence-dependency of the combined cytotoxicity was evaluated by isobologram. RESULTS: A synergistic antitumor activity of combined docetaxel + THP was exhibited against the R-27 xenograft when docetaxel was given first or simultaneously with THP. However, this synergism was diminished when THP was used before docetaxel. While an additive effect of combined docetaxel + THP was observed against MX-1 xenograft when docetaxel was given first or simultaneously with THP, this effect was not marked using the THP/docetaxel sequence. CONCLUSION: Docetaxel increased the antitumor activity of THP, but only when administered before or simultaneously with THP.

Answer 15:

Bibliographic Information

Comparative activity of four anthracyclines against heterotransplanted germ cell tumor lines. Harstrick A; Casper J; Kohne-Wompner H; Wilke H; Schmoll H J; Poliwoda H Dep. Hematology/Oncology, University of Hannover, Medical School, FRG Investigational new drugs (1990), 8 Suppl 1 S19-24. Journal code: 8309330. ISSN:0167-6997. (COMPARATIVE STUDY); Journal; Article; (JOURNAL ARTICLE) written in English. PubMed ID 1696245 AN 90337679 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

Though the majority of patients with metastatic nonseminomatous germ cell tumors can be cured by modern combination chemotherapy, for those patients who do not respond to standard therapy additional drugs are needed. The activity of three new anthracycline derivatives, 4-epidoxorubicin, THP-doxorubicin and mitoxantrone against two established human testicular cancer cell lines in comparison to doxorubicin and to cisplatin, vinblastine, bleomycin and ifosfamide was studied in a xenograft model. All drugs were given at equitoxic doses. There were no differences in antitumor activity between the four anthracycline derivatives. In line H 12.1, which is very sensitive to the standard drugs cisplatin, vinblastine, bleomycin and ifosfamide, all four anthracycline derivatives were inferior to these agents. In contrast, in line H 23.1, where all four standard agents showed a significant lower antitumor activity when compared to line H 12.1, the anthracyclines preserved their activity, indicating a lack of cross resistance. Thus the anthracycline derivatives seem to be inferior to the standard drugs as first line treatment but because of apparent lack of cross resistance they deserve

further evaluation in refractory germ cell tumors.